PATENT

Lonberg, et al. Application No.: 08/728,463 Page 2



variable region having similar affinity to a human CD4, or antigenic fragment thereof, as a human sequence immunoglobulin comprising] a variable region [comprising] having an amino acid sequence encoded by a nucleic acid with a sequence as set forth in SEQ ID NO:1, [.] SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10.

- 14. **(Amended)** The <u>monoclonal</u> human [sequence] immunoglobulin of claim 13 wherein the immunoglobulin comprises an amino acid sequence as set forth in SEQ ID NO:61 or SEQ ID NO:62.
- 22. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VH4-34 segment, a DXP'1 segment, a JH4 segment, and a heavy chain CDR3 region comprising the sequence DITMVRGPH (SEQ ID NO:63).
- 23. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VH5-51 segment, a DHQ52 segment, a JH2 segment, and a heavy chain CDR3 region comprising the sequence PANWNWYFVL (SEQ ID NO:64).
- 24. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VH4-34 segment, a JH5 segment, and a heavy chain CDR3 region comprising the sequence VINWFDP (SEQ ID NO:65).
- 25. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VH5-51 segment, a DHQ52 segment, a JH4 segment, and a heavy chain CDR3 region comprising the sequence DQLGLFDY (SEQ ID NO:66).
- 26. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VkA27/A11

Lonberg, et al. Application No.: 08/728,463

Page 3

segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQYGSSPLT (SEQ ID NO:67).

- 27. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VkL18 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQFISYPQLT (SEQ ID NO:68).
- 28. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VkL19 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQANSFPYT (SEQ ID NO:69).
- 29. (Twice Amended) A monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, comprising a VkL15 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQYDSYPYT (SEQ ID NO:70).
- 37. (Amended) An isolated monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof comprising a human sequence immunoglobulin light chain polypeptide having a VJ junction comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, and SEQ ID NO:10.
- 40. (Amended) An isolated monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or an antigenic fragment thereof comprising a human sequence immunoglobulin heavy chain polypeptide having a VDJ junction comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, and SEQ ID NO:9.
- 50. (Amended) The monoclonal human [sequence] immunoglobulin of claim 13, wherein the human sequence light chain variable region comprises an amino acid

sequence encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:10.

- 51. (Amended) The monoclonal human [sequence] immunoglobulin of claim 13, wherein the human sequence heavy chain variable region comprises an amino acid sequence encoded by SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, or SEQ ID NO:9.
- 53. (Amended) A hybridoma secreting a monoclonal human [sequence] immunoglobulin that specifically binds human CD4 or antigenic fragment thereof, wherein the immunoglobulin is selected from the group consisting of:
- a monoclonal human [sequence] immunoglobulin comprising a VH4-34 segment, a DXP'1 segment, a JH4 segment, and a heavy chain CDR3 region comprising the sequence DITMVRGPH (SEQ ID NO:63),
- a monoclonal human [sequence] immunoglobulin comprising a VH5-51 segment, a DHQ52 segment, a JH2 segment, and a heavy chain CDR3 region comprising the sequence PANWNWYFVL (SEQ ID NO:64),
- a monoclonal human [sequence] immunoglobulin comprising a VH4-34 segment, a JH5 segment, and a heavy chain CDR3 region comprising the sequence VINWFDP (SEQ ID NO:65),
- a monoclonal human [sequence] immunoglobulin comprising a VH5-51 segment, a DHQ52 segment, a JH4 segment, and a heavy chain CDR3 region comprising the sequence DQLGLFDY (SEQ ID NO:66),
- a monoclonal human [sequence] immunoglobulin comprising a VkA27/A11 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQYGSSPLT (SEQ ID NO:67),
- a monoclonal human [sequence] immunoglobulin comprising a VkL18 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQFISYPQLT (SEQ ID NO:68),